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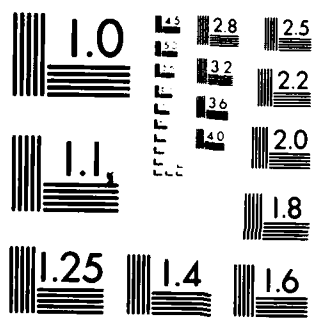


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**EFFICIENCY OF HIGH-FREQUENCY VENTILATION AS DETERMINED BY NITROGEN WASHOUTS: A MODEL STUDY.**

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We examined the frequency dependency of high-frequency ventilation (HFV) by using a two-compartment mechanical model. A loudspeaker was used as an oscillator to assist mixing between the two compartments. One compartment (C1) contained either $O_2$ or SF6 prior to mixing, while the other (C2) contained air. The rate of change of nitrogen concentration in the latter compartment was used as an index of mixing efficiency. The speaker was driven with either a sinusoidal or random signal, and the spectral characteristics and acoustic power of the pressures generated in each

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compartment were determined by a Fast Fourier Transform Analyzer and PDP 11/34 and /70 computers. Transport coefficients describing mixing increased approximately linearly with power. For a given power in C1, the mixing rates were highly frequency-dependent. The frequencies for resonance and optimal mixing were essentially identical, and decreased as gas density increased. When powers were matched in C2, however, mixing was much less dependent on frequency. Random noise proved as effective in augmenting mixing as sinusoidal excitation. It can do so while decreasing the magnitude of pressure changes in the system and while reducing the influence of changing resonant frequencies.

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## INTRODUCTION

Laboratories using a varied collection of ventilators report contradictory results in animals and man regarding ideal oscillatory frequencies and stroke volumes to be used in high-frequency ventilation (HFV) (Bohn et al., 1980; Rossing et al., 1981; Schmid, Knopp, and Rehder, 1981; Slutsky et al., 1980). We have examined the relationships between frequency, acoustic power, and gas mixing in a two-compartment mechanical model of a ventilator-lung system. This model allows the monitoring of pressures and gas composition at the site where gas mixing occurs.

The above studies had two principle aims. The first was to determine whether power delivery to the site of mixing controls mixing efficiency. Many combinations of frequency and amplitude could in principle lead to the same power when measured in the lung. The second was to evaluate the effectiveness of random noise (excitation over a broad band of frequencies) in promoting gas mixing. If mixing were monotonically related to power, and noise could be used for excitation, then the achievement of satisfactory settings on ventilators might be simplified.

## METHODS

The model (Fig. 1) was composed of two compartments, an acrylic speaker housing (compartment C1) 25 cm in diameter, with a volume of 5 liters, and a glass bottle (compartment C2) 15 cm in diameter, with a volume of 4 liters. The two compartments were joined by a cylinder 19 cm long and 3 cm in diameter.

C2 was always filled with air at the beginning of each experiment, while C1 was filled with helium, oxygen, or sulphur hexafluoride. The compartments were separated during flushing, and rejoined at the beginning of each experimental run. Once the compartments were connected, gas was sampled continuously from the distal portion of C2 and analyzed for $N_2$ content with a

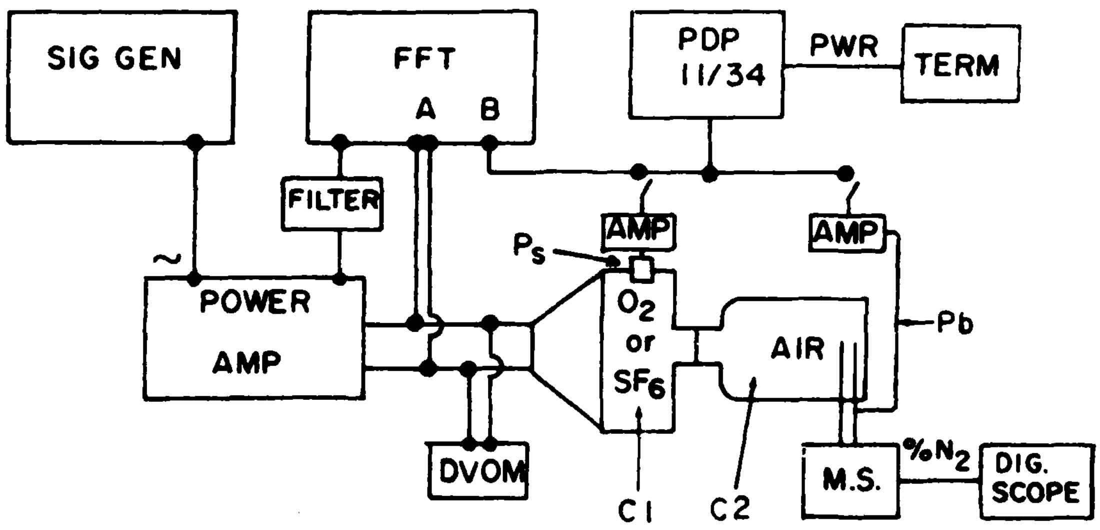


Fig. 1. Experimental setup. For description see text. Abbreviations: C1 - compartment 1, with the speaker; C2 - compartment 2; M.S. - mass spectrometer; DVOM - digital voltmeter; AMP - pressure transducer amplifiers; FFT - Fast Fourier Transform Analyzer; PDP 11/34 - DEC computer; Ps - Validyne pressure monitoring for compartment C1.

Medspec II mass spectrometer (Chemetron Corp., St. Louis, MO), or by a Med Science 505 Nitralyzer (Med Science Electronics, St. Louis, MO) when $O_2$ was used as the washout gas. The nitrogen analyzer had a sampling rate of 3 ml/min, the mass spectrometer 100 ml/min. The nitrogen concentration in C2 was recorded on a Nicolet Explorer II digital oscilloscope (Nicolet Scientific Corp., Northvale, NJ) and later transferred to DEC N11/70 and /34 computers for model and statistical analyses. The speaker was activated 15 sec after the two compartments were connected. Each experiment was 3.4 min in duration.

The speaker was driven by either a sinusoidal source (Hewlett-Packard 3311 Function Generator) or by pseudo-random binary noise generated by a Nicolet 660 Fast Fourier Transform Analyzer (Nicolet Scientific, Northvale, NJ) and filtered by a Krohn-hite 3320 digital filter (Krohn-hite, Cambridge, MA). Exciting voltages were amplified by a power amplifier and, in the case of noise, by a Gould DC amplifier (Gould Inc., Cleveland, OH) as well. The driving voltages were then directed to the coils of a 40-W, 12-in loudspeaker (Oaktron, Monroe, WI). The speaker diaphragm was coated with a thin layer of latex to reduce gas leaks; this coating raised the speaker resonant frequency from 35 to 161 Hz. Elimination of all leaks could not be accomplished without destroying the function of the speaker.

A digital voltmeter read RMS voltage across the speaker inputs. Pressures were measured by two 5F Millar PC-350 Mikro-Tip Catheter Pressure Transducers excited by TC-100 Millar Transducer Control Units (Millar Inc., Houston, TX). These units were in turn driven by a transducer amplifier (Gould Inc., Cleveland, OH). While one Millar remained fixed in the distal portion of C2, the other could be used to monitor pressures throughout the model. The fixed Millar was adjacent to the lumen of the gas sampling catheter in the mid-distal region of C2. A Statham PM131TC pressure transducer (Gould Inc., Cleveland,

OH), with diaphragm exposed, was used in C1. The transfer function describing the response of these transducers was flat within 10% over the range from 30 to 80 Hz.

The voltages applied to the speaker and the resulting pressure signals in C1 and C2 were used by the FFT analyzer to calculate and display power spectra (Bracewell, 1978), power expressed as a function of frequency. Average acoustical power ($P_{av}$) could be determined from the following relationship (Symon, 1964):

$$P_{av} = \frac{(\Delta p^2)av}{(\rho\ B)^{.5}} \qquad \langle 1 \rangle$$

where $\Delta P$ = the amplitude of a pressure wave, $\rho$ = gas density and B = the bulk modulus for the medium through which the wave is propagating. $P_{av}$ has units of energy per unit area per sec traveling in the direction n. With all else constant, acoustic power calculations made by the FFT relied solely on $\Delta P$ as measured by the appropriate transducer.

Power spectra were averaged from 16 samples, each sample consisting of 4 sec of pressure recording. Total power ($P_{TOT}$), representing a summation of the power at each of 1046 points spread equally across a frequency range from 0 to 100 Hz, was used to compare random and sinusoidal inputs. Transfer functions (Hab) for the physical system between two transducers were calculated by the analyzer from the power spectra recorded in both compartments. These functions are expressed in the following equation:

$$Hab = Gab/Gaa \qquad \langle 2 \rangle$$

where Gab is the average cross-spectrum between the input a(t) and output b(t). The cross-spectrum, rather than the power spectrum, of b(t) must be used in the numerator to insure that the derived transfer function represents a linear system; that is, the measured output is due only to the known input and not

some other unobserved variable. This distinction is most important when transfer functions for the respiratory system, a notably alinear system, are obtained. Gaa is the power spectrum of a(t) (Bracewell, 1978). Pressure signals were also processed by a PDP-11/34 computer for time averaging.

A Marquardt least-squares regression (Marquardt, 1963) was used to fit the gas mixing data to a mathematical model consisting of equations for a two-compartment, open system (Appendix).

RESULTS

Fig. 2 shows the change in nitrogen concentration in C2, when C1 contained $O_2$ and mixing was induced by operating the speaker. In this example, C1 initially contained only oxygen, and the speaker was driven at 51 Hz at 80% of the maximum power tolerated by the speaker. The foam suspension for the speaker diaphragm was permeable, accounting for the rise in $N_2$ near the end of some washouts. Our mathematical model included an expression for the loss ($K_\ell$) of tracer ($O_2$ or SF6) from C1.

For a set power and driving frequency, nitrogen mixing curves were superimposable. When the speaker remained off, mixing induced by both diffusion and the convective pull of the gas analyzers was relatively small (Fig. 3). When fixed RMS voltages were applied to the speaker at a succession of frequencies, an optimum frequency was found. A smoke plume within C2 revealed extreme turbulence when the speaker was driven at the optimal frequency.

The coefficient of transport ($T_c$) from C1 to C2 was estimated by a least-squares fit to the mixing data (Appendix). These coefficients are plotted in Fig. 4 against various frequencies and powers in C1. For a given coefficient the required input power varied widely with changing frequencies. At 70 Hz, for example, voltages that would have destroyed the speaker would

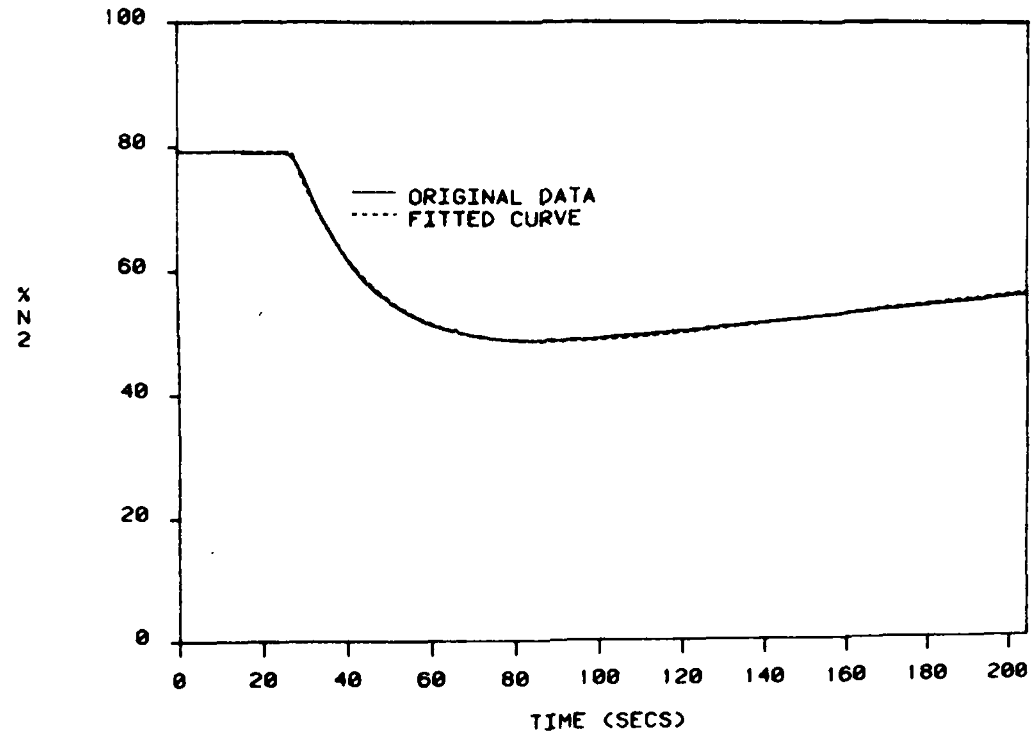


Fig. 2. A nitrogen mixing curve with gas sampling from C2, using sinusoidal excitation at 50 Hz. $O_2$ was the diluting gas. The data and mathematical fit for a two-compartment, open system are superimposable.

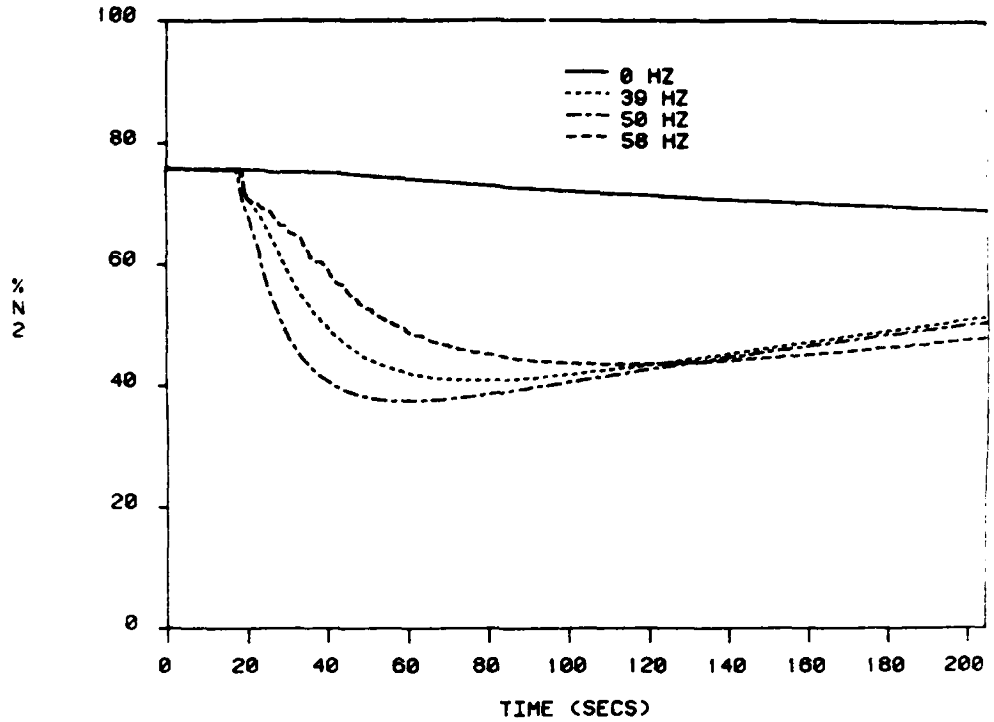


Fig. 3. Mixing curves in an $O_2$-$N_2$ environment with a fixed driving voltage of 10 V RMS. An optimal frequency of 50 Hz is evident.

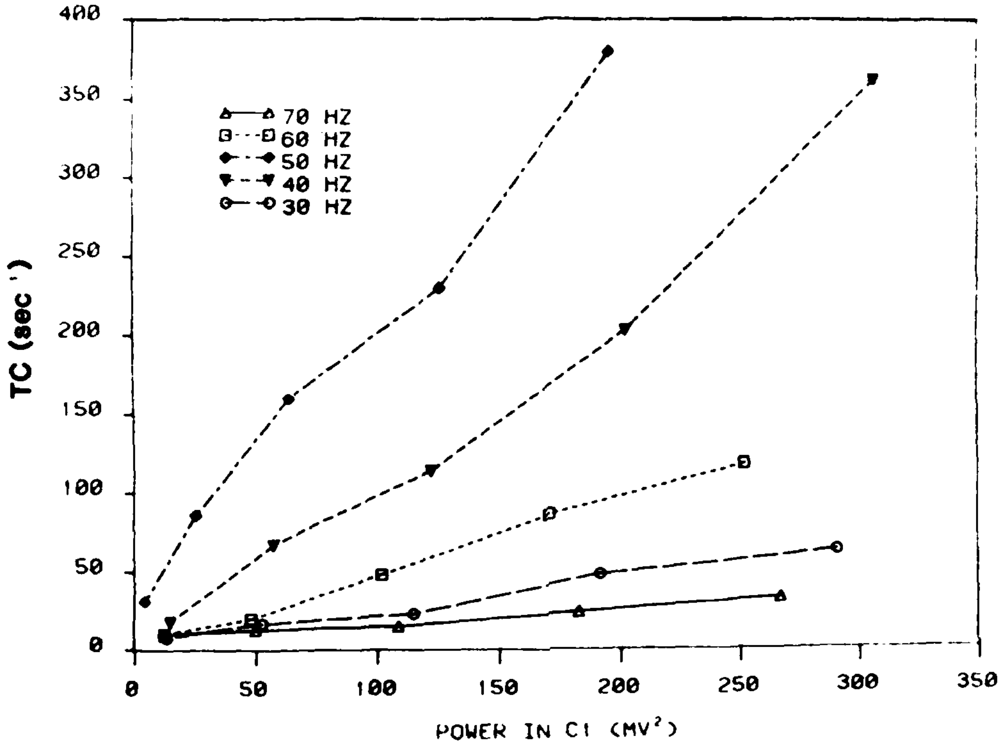


Fig. 4. Transport coefficients (Tc), derived from a least-squares fit of the $O_2$-$N_2$ mixing data to a model of a two-compartment, open system, are plotted against power in C1.

have been required to achieve appreciable mixing.

Pronounced frequency dependencies were due to the shape of the system transfer functions (Fig. 5). These functions were obtained by applying random noise over the frequency range from 1 to 100 Hz, and comparing the resultant pressures in C1 and C2. Increasing gas density caused a progressive reduction in resonant frequency from 63 to 35 Hz. The pressure waves passing through the connector were so effective near the resonant frequency that mixing stimulated by other frequencies seemed slight in comparison.

Overall system transfer functions relating speaker driving voltages to the pressures in C2 were almost identical to those illustrated in Fig. 5, indicating that the impedance of the speaker had little to do with the overall system properties for the frequency range examined. Measurement of the impedance across C2 was attempted by placing the movable Millar pressure transducer at the proximal end of C2 and comparing its output to that from the fixed, distal Millar. This impedance was too low to be measured; the transfer function approximated 1 for the frequency range 1 - 100 Hz.

When coefficients for mixing of nitrogen and oxygen were plotted against power measured in C2 (Fig. 6), we found that the most effective frequencies were the higher ones. For a given coefficient of mixing, however, the power required to achieve those mixing rates varied less with frequency than in the case of powers measured in C1.

When total powers ($P_{TOT}$) in C2 were matched (Fig. 7), and $O_2$ was initially in C1, the initial rate of loss of $N_2$ from C2 was similar for both random noise (40 to 70 Hz band-pass filtered) and sinusoidal excitation at 49 Hz. (Fig. 8). The same was true when SF6 and air were mixed by applying matched powers for noise and sinusoidal excitation (Fig. 9). Nevertheless, sinusoidal forcing resulted in a delay in initiation of mixing with SF6 that was 2 sec longer than

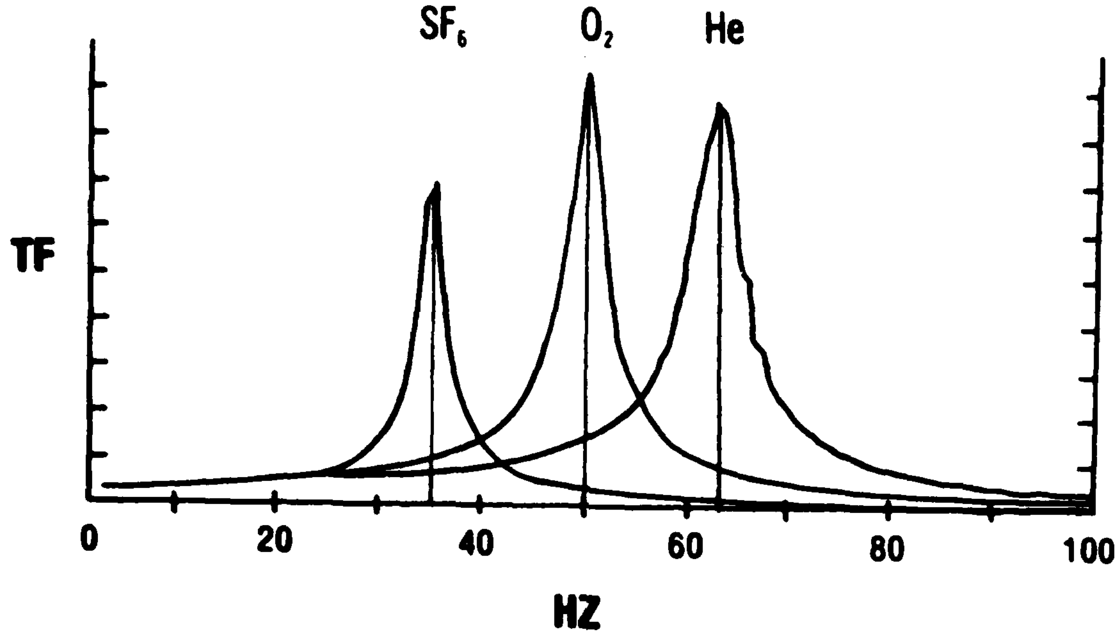


Fig. 5. The influence of gas density on resonant frequencies is illustrated by the transfer function (TF = Hab of Eq. 1) relating C2 to C1. The gases used in C1 were, from left to right, SF6, $O_2$, and He.

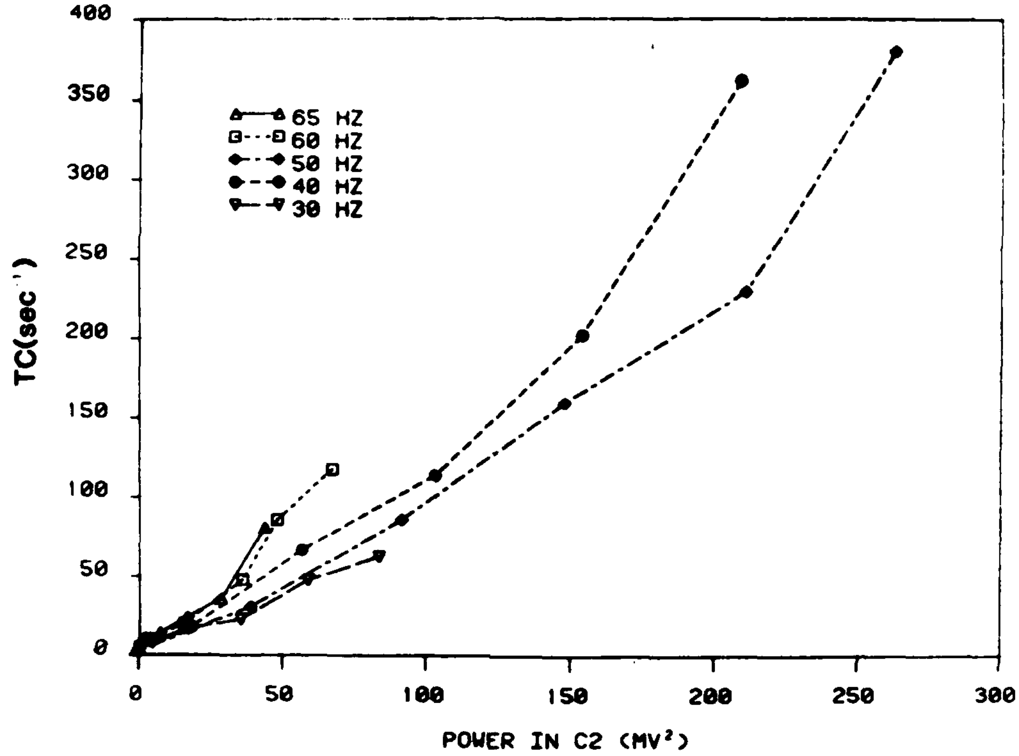


Fig. 6. The transport coefficients found in Fig. 4 are related to the power measured in C2.

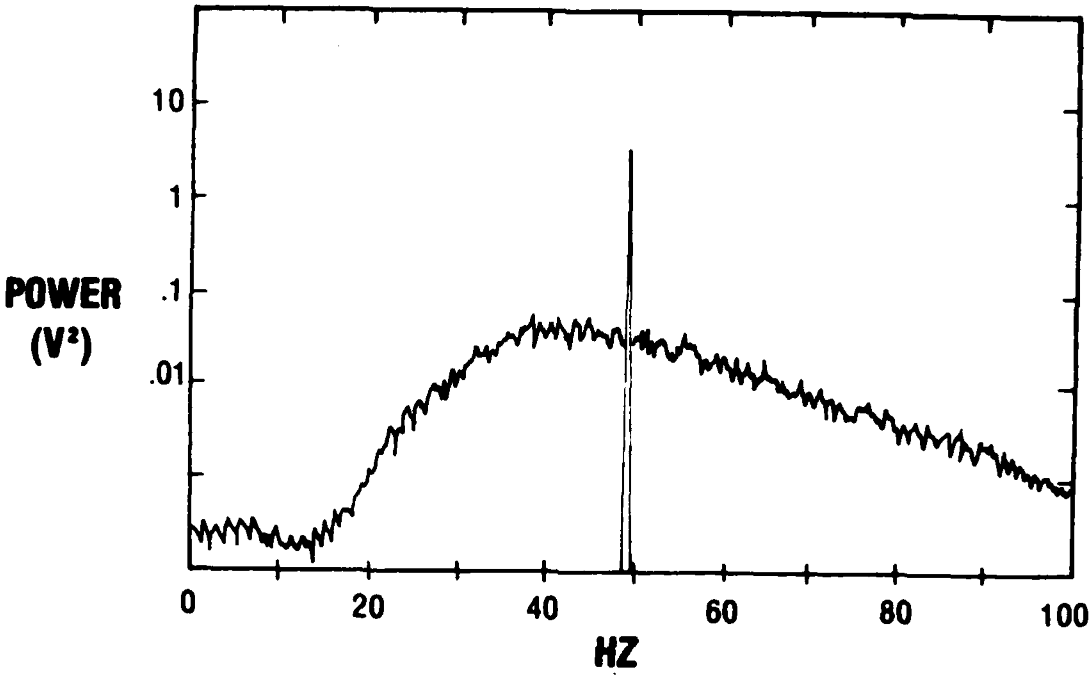


Fig. 7. The power spectra measured in C2 under both sinusoidal and noise excitation are compared. The noise is bandpass filtered from 40 to 70 Hz. The total powers in C2 ($P_{TOT}$, the summation of power across frequencies from 0 to 100 Hz) were made identical for both forms of excitation.

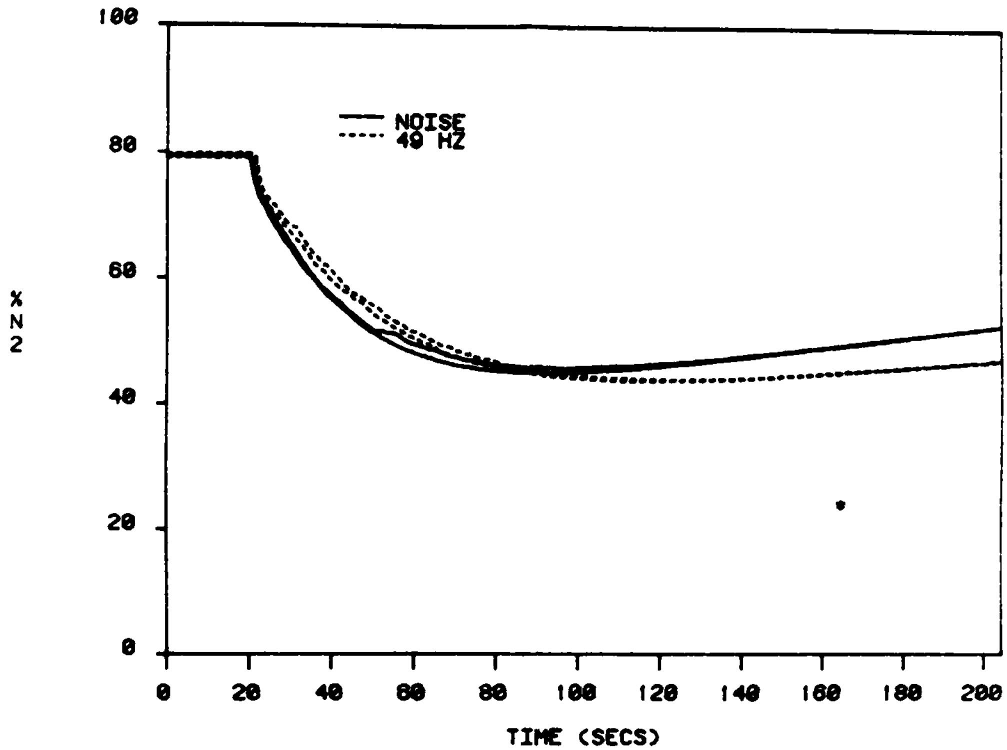


Fig. 8. Filtered noise and sinusoidal excitation produce washouts that are similar under conditions of matched total power in C2.

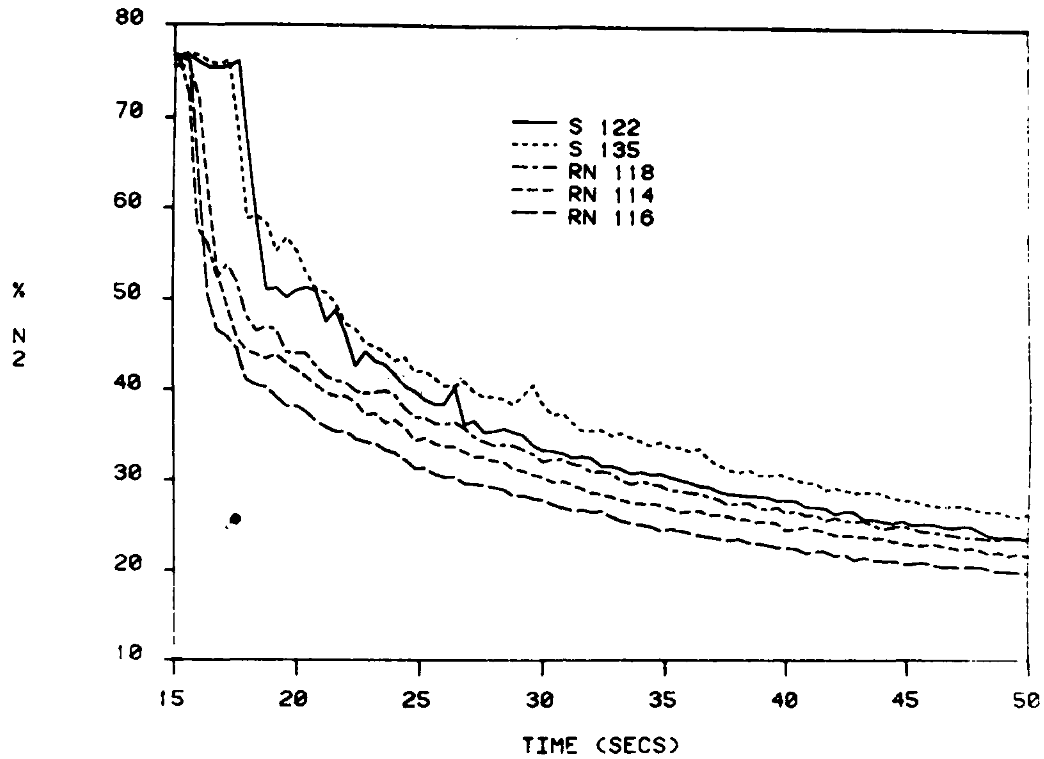


Fig. 9. A comparison of sinusoidal and random noise excitation as a means of inducing mixing in an SF6-air environment. S = sinusoidal input; RN = random noise. Values of total power ($mv^2$) are given for each curve. The delay in mixing for sinusoidal forcing is genuine and unexplained.

when random noise was used. [$\text{latency}_{\text{noise}} = 15.7 \pm 0.5$ s (n=3); $\text{latency}_{\text{sine}} = 17.5 \pm 0.4$ s (n = 4); $P < 0.005$]. The % nitrogen curve did not rise during these tests, presumably due to the poor diffusibility of SF6 through leaks in C1.

DISCUSSION

Since the impedance across C2 was immeasurably small, the power dissipated in C2 must have been small. Nevertheless, the result of that power dissipation, convective mixing, was clearly dependent on the power delivered to C2.

While we would have liked to extend the power ranges measured in C2 for frequencies other than 40 and 50 Hz (Fig. 6), this was not possible due to the restrictions on power input to the speaker (40 W) and the narrow band-pass characteristics of the connector. Nevertheless, for low rates of mixing, matching power at the site of mixing removes much of the frequency dependency. For example, to maintain a given rate of gas mixing ($T_c = 50\ \text{sec}^{-1}$) while shifting from 50 to 30 Hz (Fig. 4), power in C1 had to increase more than 20 times. In contrast, the power required in C2 changed no more than twofold for the same change in frequency (Fig. 6).

When power was matched in C2, mixing generally was more rapid at higher frequencies, just as would be predicted if we assume peak flows followed peak pressures (Slutsky, 1980). We did note, however, that for a given power in C2, 40 Hz resulted in faster mixing than did 50 Hz. We have no explanation for this observation.

The reported optimal frequencies for HFV (Bohn et al., 1980; Rossing et al., 1981) may simply result from equipment and anatomical impedances. A similar suggestion has been made by Schmid, Knopp, and Rehder, 1981. Since impedance is a function of ventilator design, tubing geometry, and gas density,

as well as anatomy, a universal, ideal oscillatory frequency should not be expected.

There remains a need to determine the effectiveness of HFV in some rapid, convenient manner. This work suggests that the measurement of airway oscillatory pressures as close to the site of gas exchange as possible may yield the needed information. In animals, a piezoelectric catheter transducer can be inserted down an endotracheal tube, thus allowing high frequency measurements in the lower trachea. It may be that accelerometer measurements on the chest wall may eventually yield information on the power delivered to alveoli, once due account is made of chest wall impedances and energy transmission from the larger airways. Nitrogen washout curves may be a further means of quickly assessing the effectiveness of HFV.

Random noise exhibits several useful characteristics. If the resonant properties of a ventilatory circuit are such that driving frequency is critical, and that frequency is apt to change for one reason or another, than random noise provides increased latitude in setting ventilatory parameters.

If different paths through the pulmonary tree have different resonant properties, the use of a broad band of frequencies may be far more effective in promoting gas exchange than any single frequency at the same input power.

Another property of random noise is illustrated in Fig. 10. Records of random and sinusoidal pressure wave forms are shown for the condition of matched total power in C2. The sinusoid had peak to peak pressure excursions of 15 cm $H_2O$. The random noise had more pressure swings for the same time interval (more than three times), but the mean pressure excursion was only 5 cm $H_2O$. Only 2% of those excursions had pressures above 12 cm $H_2O$, and only 15% had pressures greater than 10 cm $H_2O$. Indeed, it is the nature of sinusoids that their most probable amplitudes are their extremes, whereas the most

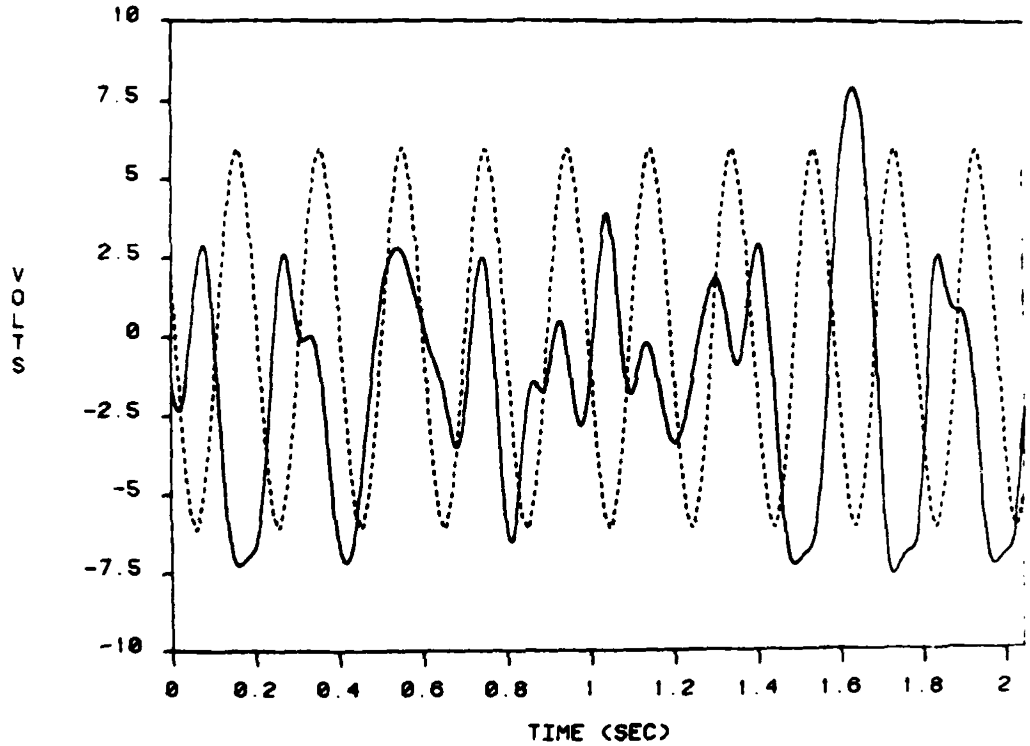


Fig. 10. Pressure versus time comparison for sinusoidal (dashed line) and random noise (solid line) excitation. Total powers in C2 were matched. The noise was bandpass filtered between 40 and 70 Hz.

probable amplitudes for noise are close to the median, in this case, zero (Bracewell, 1978). If one wishes to minimize the mechanical effects of oscillations on airways by minimizing the magnitude of pressure changes, random noise would seem to have a clear advantage over sinusoidal forcing.

Power, or something akin to it, can be monitored quite simply. An audio range voltmeter provides RMS voltage that is proportional to the square root of power for sinusoidal signals. For random noise inputs, an AC voltmeter was not useful; instead we used the time average of squared voltages from the pressure transducers. The time average correlated well with power found by averaging in the frequency domain, and involved simpler equipment and computations.

SUMMARY

In our model we saw nothing to refute the concepts expressed by Bohn et al., 1980, relating enhancement of diffusibility to increasing frequency monotonically (Fig. 7). In our model, however, the first requirement was for power delivery to the site of mixing. Power delivery was in turn affected by impedances between the oscillator and the mixing site. When there is neither a detailed knowledge of system impedances nor measurements of power at the site of mixing, inferences about frequency dependence of high-frequency ventilation must be suspect.

Lastly, questions of optimal frequency may be sidestepped by the use of noise for power gas mixing. Certain theoretical and practical advantages accrue from this mode of mixing.

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Riggs, 1963, provides equations derived from Skinner et al., 1959, describing the appearance of a tracer ($O_2$ or SF6 in our case) in the second of two compartments (C2), after introducing the tracer to the first compartment (C1). The tracer is transported to C2 at a rate determined by the transport coefficient ($T_c$). (Transport from C2 to C1 was assumed to be governed by the same coefficient.) The derived values for $T_c$ would have been somewhat lower and related in a complicated fashion with power if we had not taken into account the leakage of oxygen from C1. The rise of nitrogen concentration in C2 during the latter part of experimental runs with oxygen was influenced by both $K_1$ (the leak in C1) and $T_c$. Least-squares regression was used to solve the following equation for both $K_1$ and $T_c$.

$$\% N_2 = (1 - F_{c2.t}) \times 100$$

where $F_{c2.t}$ is the fraction of tracer appearing with time in C2. $F_{c2.t}$ is expressed as:

$$F_{c2.t} = \frac{T_c}{G} \left\{ e^{[-1/2(2T_c + K_1 - G)t]} - e^{[-1/2(2T_c + K_1 - G)t]} \right\}$$

where $G = \sqrt{K_1^2 + 4(T_c)^2}$

When $K_1$ is zero, the above equation reduces to a single exponential.

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